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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,966	12/20/2007	**Shuji Sakuma**	3462.1019-000	6665

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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1613	

MAIL DATE	DELIVERY MODE
10/13/2010	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,966	SAKUMA ET AL.	
	Examiner	Art Unit	
	ERNST V. ARNOLD	1613	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 September 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-6 and 8-20* is/are pending in the application.

4a) Of the above claim(s) *11-19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6,8-10 and 20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/29/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim 7 has been cancelled. Claims 11-20 are new. Claims 1-6 and 8-20 are pending and under examination. Applicant's amendments have necessitated a new ground of rejection. Accordingly, this Action is FINAL.

Election/Restrictions

Newly submitted claims 11-19 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: claims 11-19 are directed to a method of reducing toxicity of an antitumor agent without reducing the antitumor effects. Inventions Group I, claims 1-6, 8-10 and 20, and Group II, claims 11-19 are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case the method of reducing the toxicity of an antitumor agent can be performed with the antitumor agent in a sustained release porous particulate preparation not comprising hydroxyapatite.

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder.

All claims directed to a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 11-19 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claims 1-6, 8-10 and 20 are under examination.

Withdrawn rejections:

Applicant's amendments and arguments filed 9/29/10 are acknowledged and have been fully considered. Any rejection and/or objection not specifically addressed below is herein withdrawn. Applicant has amended claim 1 to recite particles having a maximum size of 5 μm. This amendment overcomes the following rejections:

1. Claims 1-10 are rejected under 35 U.S.C. 102(b) as being anticipated by Aoki et al. (ref C1 on the IDS filed on 12/20/07).
2. Claims 1-3, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by JP4112832 (reference B4).
3. Claims 1-3, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Mohri et al. (Jpn J Cancer Chemother 1999, 26(12), 1791-1793) (reference C3 but the Examiner has supplied an English translation).
4. Claims 1-3 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Nakatani et al. (Jpn J Cancer Chemother 1992, 19(10), 1644-1647) (reference C4 but the Examiner has supplied an English translation).

These rejections are properly withdrawn.

The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set of rejections and/or objections presently being applied to the instant application.

Information Disclosure Statement

The information disclosure statement (IDS) submitted on 9/29/10 was filed after the mailing date of the office action on 4/30/10. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-10 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Aoki et al. (ref C1 on the IDS filed on 12/20/07).

Aoki et al. disclose adsorbtion of doxorubicin, mitomycin C (an antitumor antibiotic) and fluoroyracil on hydroxyapatite microcrystals (Abstract and Page 4, 2.4). The crystals were less than 0.1 micron in size (page 5, 3.2). The amount of doxorubicin adsorbed was 0.2 mg per 1 mg of hdyroxyapatite (page 6, 3.4). Since the components taught in the art are the same as instantly claimed then the composition of Aoki et al.

inherently has the same properties as instantly claimed such as reduced toxicity while maintaining antitumor effects as compared to the toxicity of the antitumor agent administered without the hydroxyapatite particles. The principle of law states that: "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Blending the antitumor agent with the hydroxyapatite particles reads on a product by process. Please note that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

With regard to claims 2 and 20, it is noted that the reference does not teach that the composition can be used in the manner instantly claimed, **oral formulation or orally administered**, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a

structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

With regard to claims 10 and 20, please note that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Therefore, instant claims 1-6, 8-10 and 20 are anticipated.

Response to arguments:

Applicant asserts that Aoki et al. does not disclose whether the presence of HA particles reduces toxicity of adriamycin. However, this is an inherent property as asserted by the Examiner above. These arguments are not persuasive.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-6, 8-10 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Lee et al. (WO 02/41844) (reference B1).

Lee et al. disclose compositions of nanocrystalline calcium phosphate paste with anti-cancer agents thus anticipating instant claims 1-4 (Abstract; pages 13-16 and claims 22-41). Lee et al. teach particle size ranging from 5 nm to 150 nm thus anticipating instant claims 5-8. The amount of anti-cancer drug is from about 0.01 to 10% by weight of the composition which means the rest is hydroxyapatite thus anticipating instant claim 9. Since the components taught in the art are the same as instantly claimed then the composition of Lee et al. inherently has the same properties as instantly claimed such as reduced toxicity while maintaining antitumor effects as compared to the toxicity of the antitumor agent administered without the hydroxyapatite particles. The principle of law states that: "A chemical composition and its properties are inseparable. Therefore, if the prior art teaches the identical chemical structure, the properties applicant discloses and/or claims are necessarily present." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990).

Blending the antitumor agent with the hydroxyapatite particles reads on a product by process. Please note that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). As a

practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

With regard to claim 2 and 20, it is noted that the reference does not teach that the composition can be used in the manner instantly claimed, **oral formulation or orally administered**, however, the intended use of the claimed composition does not patentably distinguish the composition, per se, since such undisclosed use is inherent in the reference composition. In order to be limiting, the intended use must create a structural difference between the claimed composition and the prior art composition. In the instant case, the intended use does not create a structural difference, thus the intended use is not limiting.

With regard to claims 10 and 20, please note that in product-by-process claims, "once a product appearing to be substantially identical is found and a 35 U.S.C. 102 rejection [is] made, the burden shifts to the applicant to show an unobvious difference." MPEP 2113. This rejection under 35 U.S.C. 102 is proper because the "patentability of a product does not depend on its method of production." *In re Thorpe*, 227 USPQ 964, 966 (Fed. Cir. 1985). As a practical matter, the Patent Office is not equipped to manufacture products by the myriad of processes put before it and then obtain prior art products and make physical comparisons therewith." *In re Brown*, 459 F.2d 531, 535, 173 USPQ 685, 688 (CCPA 1972).

Therefore, instant claims 1-6, 8-10 and 20 are anticipated.

Response to arguments:

Applicant asserts that Lee does not teach the use of HA particles to reduce toxicity of the antitumor agent. However, such properties are inherent in the composition of Lee as discussed above. Applicant argues that the composition of Lee is a cement or paste that sets into a product. However, such a composition could be administered orally especially, for example, if a bone cancer of the jaw was being treated.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-6, 8-10 and 20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lee et al. (WO 02/41844) (reference B1).

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of

the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Applicant claims an antitumor agent.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The reference of Lee et al. is discussed in detail above and that discussion is hereby incorporated by reference.

Ascertainment of the difference between the prior art and the claims

(MPEP 2141.02)

1. The difference between the instant application and Lee et al. is that Lee et al. do not expressly teach all of the antitumor agents in instant claims 3 and 4. This deficiency in Lee et al. is cured by common sense.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to add any antitumor/anticancer agent under the sun to the composition of Lee et al. and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Lee et al. directs one of ordinary skill in the art to add anti-cancer agents to the composition which would include each and every known anti-cancer agent known to the artisan. The expected and predictable result is an antitumor/anticancer composition.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Response to arguments:

Applicant asserts that the surprising and unexpected results throughout the specification which are supported by empirical evidence that HA particles are better at reducing toxicity than calcium triphosphate. However, the art also teaches using HA and the same reduction in toxicity would be observed. These arguments are not persuasive.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-6, 8-10 and 20 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-8 and 11 copending Application No. 11/887710. The instant subject matter embraces or is embraced by the subject matter of the copending application. The copending application teaches an antitumor composition comprising a antitumor component combined with hdyroxyapatite particles less than 0.1 micron in size.

The copending application does not expressly disclose pulverizing the composition. However, pulverizing medicinal preparations for use is obvious to one of ordinary skill in the art of pharmaceutical preparation.

Therefore, the Examiner concludes that one of ordinary skill in the art would have recognized the obvious variation of the instant application over the copending application.

This is a provisional obviousness-type double patenting rejection.

Response to arguments:

Applicant will consider filing a terminal disclaimer once allowable subject matter is identified. Until that time the claims remain rejected.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ERNST V. ARNOLD whose telephone number is (571)272-8509. The examiner can normally be reached on M-F 7:15-4:45.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Ernst V Arnold/
Primary Examiner, Art Unit 1616